

WHAT IS CLAIMED IS:

1. A method of prevention or inhibition of uncontrolled proliferation and spreading or migration of a metastatic neoplastic cell of a cancer in a mammal, comprising administration to the mammal of a therapeutically effective amount of a pharmaceutical composition comprising a cell-permeable fusion protein conjugate comprising a polypeptidic cell-membrane transport moiety and a Clostridium botulinum C3 exotransferase unit, or a functional analog thereof.
2. A method of prevention or inhibition of uncontrolled proliferation and spreading or migration, within a resection margin of a host tissue proximal to the site of excision of a tumor of a cancer in a mammal, of a metastatic neoplastic cell residing in the resection margin, comprising administration of a therapeutically effective amount of a pharmaceutical composition comprising a cell-permeable fusion protein conjugate comprising a polypeptidic cell-membrane transport moiety and a Clostridium botulinum C3 exotransferase unit, or a functional analog thereof, said administration being directly on to the surface of the resection margin or below the surface of the resection margin or into the tissue proximal to the resection margin which remains in the mammal, said administration in a time interval prior to or subsequent to or prior to and subsequent to excision or removal of the tumor.
3. A method of prevention of growth of a tumor from a malignant cell in a host tissue in a mammal comprising administration to the mammal of a therapeutically effect amount of a pharmaceutical composition comprising a cell-permeable fusion protein conjugate comprising a polypeptidic cell-membrane transport moiety and a Clostridium botulinum C3 exotransferase unit, or a functional analog thereof, wherein the fusion protein simultaneously prevents or inhibits at least two of malignant cell migration, malignant cell proliferation, angiogenesis or tubular structure formation or capillary network growth proximal to the malignant cell, and secretion of an active metalloproteinase from the malignant cell.

4. A method of prevention of growth within a resection margin of a host tissue proximal to a site of excision or removal of a first tumor of a cancer in a mammal, of a second tumor comprising a residual tumor cell of the cancer, the method comprising administration of a therapeutically effective amount of a pharmaceutical composition comprising a cell-permeable fusion protein conjugate comprising a polypeptidic cell-membrane transport moiety and a Clostridium botulinum C3 exotransferase unit, or a functional analog thereof, said administration being directly on to the surface of the resection margin or below the surface of the resection margin or into the tissue proximal to the resection margin which remains in the mammal, and said administration being in a time interval prior to, or subsequent to, or both prior to and subsequent to excision or removal of the first tumor, wherein the fusion protein simultaneously prevents or inhibits at least two of residual tumor cell migration, residual tumor cell proliferation, angiogenesis or tubular structure formation or capillary network growth proximal to the residual tumor cell, and secretion of an active metalloproteinase from the residual tumor cell.
5. The method of claim 1, wherein the fusion protein conjugate is BA-05.
6. The method of claim 1, wherein the cancer is selected from the group consisting of breast, brain, colon, skin, kidney, and hepatic cancer.
7. The method of claim 1, wherein the cancer is a brain tumor selected from the group consisting of glial tumors, neuron tumors, pineal gland tumors, menigeal tumors, tumors of nerve sheath, lymphomas, malformative tumors, and metastatic tumors located in the brain derived from tumors of the lung, breast, melanoma, kidney, and gastrointestinal tract.
8. The method of claim 1, wherein the cancer is a brain tumor selected from the group consisting of anaplastic astrocytoma, glioblastoma multiform, pilocytic astrocytoma, oligodendroglioma, ependymoma, myxopapillary ependymoma, subependymoma, choroid plexus papilloma, neuroblastoma, ganglioneuroblastoma, ganglioneuroma, and medulloblastoma, pineoblastoma and pineocytoma, meningioma, meningeal hemangiopericytoma, meningeal

sarcoma, Schwannoma (neurolemmoma) and neurofibroma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, primary and secondary subtypes of Hodgkin's lymphoma, primary and secondary subtypes of non-Hodgkin's lymphoma, craniopharyngioma, epidermoid cysts, dermoid cysts and colloid cysts.

9. The method of claim 1, wherein the therapeutically effective amount is about 0.001 micrograms per cc to about 50 micrograms per cc of tissue.
10. The method of claim 1, wherein the therapeutically effective amount is about 0.0001 micrograms of fusion protein per cubic centimeter (cc) of tissue to about 100 micrograms per cubic centimeter of tissue.
11. The method of claim 1, wherein the therapeutically effective amount is about 1 micrograms per milliliter to about 10 micrograms per milliliter to about 50 micrograms per milliliter.
12. The method of claim 1, wherein the administration is by injection, by topical application, or by implantation.
13. The method of claim 1, wherein the administration is selected from the group consisting of intrarticular, intraocular, intranasal, intraneural, intradermal, intraosteal, sublingual, oral, topical, intravesical, intrathecal, intravenous, intraperitoneal, intracranial, intramuscular, subcutaneous, inhalation, atomization and inhalation, application directly into a tumor, application directly into a disease site, application directly on or into the margins remaining after resection of a tumor, enteral, enteral together with a gastroscopic procedure, and ECRP.
14. The method of claim 1, wherein the polypeptidic cell-membrane transport moiety comprises a peptide containing from about 5 to about 50 amino acids.
15. The method of claim 1, wherein the Clostridium botulinum C3 exotransferase unit comprises the amino acid sequence designated by the sequence of fusion protein BA-05.

16. The method of claim 1, wherein the functional analog comprises a protein exhibiting activity in the range of 50% to 500% of that of wild type *Clostridium botulinum* C3 exotransferase.
17. The method of claim 1, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier.
18. The method of claim 1, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier selected from the group consisting of poly(ethylene-co-vinyl acetate), PV A, partially hydrolyzed poly(ethylene-co-vinyl acetate), poly(ethylene-co-vinyl acetate-co-vinyl alcohol), a cross-linked poly(ethylene-co-vinyl acetate), a cross-linked partially hydrolyzed poly(ethylene-co-vinyl acetate), a cross-linked poly(ethylene-co-vinyl acetate-co-vinyl alcohol), poly-D,L-lactic acid, poly-L-lactic acid, polyglycolic acid, PGA, copolymers of lactic acid and glycolic acid, polycaprolactone, polyvalerolactone, poly (anhydrides), copolymers of polycaprolactone with polyethylene glycol, copolymers of polylactic acid with polyethylene glycol, polyethylene glycol; and combinations and blends thereof.
19. The method of claim 1, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier comprising an aqueous gelatin, an aqueous protein, a polymeric carrier, a cross-linking agent, and a combination thereof.
20. The method of claim 1, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier comprising a matrix.
21. The method of claim 1, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier comprising water, a pharmaceutically acceptable buffer salt, a pharmaceutically acceptable buffer solution a pharmaceutically acceptable antioxidant, ascorbic acid, one or more low molecular weight pharmaceutically acceptable polypeptide, a peptide comprising about 2 to about 10 amino acid residues, one or more pharmaceutically acceptable protein, one or more pharmaceutically acceptable

amino acid, an essential-to-human amino acid, one or more pharmaceutically acceptable carbohydrate, one or more pharmaceutically acceptable carbohydrate-derived material, a non-reducing sugar, glucose, sucrose, sorbitol, trehalose, mannitol, maltodextrin, dextrans, cyclodextrin, a pharmaceutically acceptable chelating agent, EDTA, DTPA, a chelating agent for a divalent metal ion, a chelating agent for a trivalent metal ion, glutathione, pharmaceutically acceptable nonspecific serum albumin, and combinations thereof.

22. The method of claim 1, wherein the pharmaceutical composition is sterile.
23. The method of claim 1, wherein the pharmaceutical composition is sterilizable.
24. The method of claim 1, wherein the pharmaceutical composition is sterilized.
25. The method of claim 1, wherein the pharmaceutical composition is in a vial in a unit dosage amount or in an integral multiple of a unit dosage amount.
26. The method of claim 1, wherein the pharmaceutical composition is dried.
27. The method of claim 1, wherein the pharmaceutical composition comprises a dehydrated matrix.
28. The method of claim 1, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier.
29. The method of claim 1, wherein the pharmaceutical composition comprises a fusion protein in a lyophilized matrix.
30. Use of a pharmaceutical composition comprising a cell-permeable fusion protein conjugate comprising a polypeptidic cell-membrane transport moiety and a *Clostridium botulinum* C3 exotransferase unit, or a functional analog thereof, for preventing or inhibiting uncontrolled proliferation and spreading or migration of a metastatic neoplastic cell of a cancer in a mammal.

31. Use of a pharmaceutical composition comprising a cell-permeable fusion protein conjugate comprising a polypeptidic cell-membrane transport moiety and a *Clostridium botulinum* C3 exotransferase unit, or a functional analog thereof, for preventing or inhibiting uncontrolled proliferation and spreading or migration, within a resection margin of a host tissue proximal to the site of excision of a tumor of a cancer in a mammal, of a metastatic neoplastic cell residing in the resection margin.
32. Use of a pharmaceutical composition comprising a cell-permeable fusion protein conjugate comprising a polypeptidic cell-membrane transport moiety and a *Clostridium botulinum* C3 exotransferase unit, or a functional analog thereof, for preventing growth of a tumor from a malignant cell in a host tissue in a mammal, wherein the fusion protein simultaneously prevents or inhibits at least two of malignant cell migration, malignant cell proliferation, angiogenesis or tubular structure formation or capillary network growth proximal to the malignant cell, and secretion of an active metalloproteinase from the malignant cell.
33. Use of a pharmaceutical composition comprising a cell-permeable fusion protein conjugate comprising a polypeptidic cell-membrane transport moiety and a *Clostridium botulinum* C3 exotransferase unit, or a functional analog thereof, for preventing growth within a resection margin of a host tissue proximal to a site of excision or removal of a first tumor of a cancer in a mammal, of a second tumor comprising a residual tumor cell of the cancer, wherein the fusion protein simultaneously prevents or inhibits at least two of residual tumor cell migration, residual tumor cell proliferation, angiogenesis or tubular structure formation or capillary network growth proximal to the residual tumor cell, and secretion of an active metalloproteinase from the residual tumor cell.
34. The use of any one of claims 30 to 33, wherein the fusion protein conjugate is BA-05.
35. The use of claim 30, 31 or 33, wherein the cancer is selected from the group

consisting of breast, brain, colon, skin, kidney, and hepatic cancer.

36. The use of claim 35, wherein the cancer is a brain tumor selected from the group consisting of glial tumors, neuron tumors, pineal gland tumors, menigeal tumors, tumors of nerve sheath, lymphomas, malformative tumors, and metastatic tumors located in the brain derived from tumors of the lung, breast, melanoma, kidney, and gastrointestinal tract.
37. The use of claim 35, wherein the cancer is a brain tumor selected from the group consisting of anaplastic astrocytoma, glioblastoma multiform, pilocytic astrocytoma, oligodendroglioma, ependymoma, myxopapillary ependymoma, subependymoma, choroid plexus papilloma, neuroblastoma, ganglioneuroblastoma, ganglioneuroma, and medulloblastoma, pineoblastoma and pineocytoma, meningioma, meningeal hemangiopericytoma, meningeal sarcoma, Schwannoma (neurolemmoma) and neurofibroma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, primary and secondary subtypes of Hodgkin's lymphoma, primary and secondary subtypes of non-Hodgkin's lymphoma, craniopharyngioma, epidermoid cysts, dermoid cysts and colloid cysts.
38. The use of any one of claims 30 to 37, wherein the pharmaceutical composition is formulated for a dosage form of about 0.001 micrograms per cc to about 50 micrograms per cc of tissue.
39. The use of any one of claims 30 to 37, wherein the pharmaceutical composition is formulated for a dosage form of about 0.0001 micrograms of fusion protein per cubic centimeter (cc) of tissue to about 100 micrograms per cubic centimeter of tissue.
40. The use of any one of claims 30 to 37, wherein the pharmaceutical composition is formulated for a dosage form of about 1 micrograms per milliliter to about 10 micrograms per milliliter to about 50 micrograms per milliliter.
41. The use of any one of claims 30 to 40, wherein the pharmaceutical

composition is formulated for injection, topical application, or implantation.

42. The use of claim 1, any one of claims 30 to 40, wherein the pharmaceutical composition is formulated for an administration mode selected from the group consisting of intrarticular, intraocular, intranasal, intraneural, intradermal, intraosteal, sublingual, oral, topical, intravesical, intrathecal, intravenous, intraperitoneal, intracranial, intramuscular, subcutaneous, inhalation, atomization and inhalation, application directly into a tumor, application directly into a disease site, application directly on or into the margins remaining after resection of a tumor, enteral, enteral together with a gastroscopic procedure, and ECRP.
43. The use of any one of claims 30 to 42, wherein the polypeptidic cell-membrane transport moiety comprises a peptide containing from about 5 to about 50 amino acids.
44. The use of any one of claims 30 to 43, wherein the *Clostridium botulinum* C3 exotransferase unit comprises the amino acid sequence designated by the sequence of fusion protein BA-05.
45. The use of any one of claims 30 to 44, wherein the functional analog comprises a protein exhibiting activity in the range of 50% to 500% of that of wild type *Clostridium botulinum* C3 exotransferase.
46. The use of any one of claims 30 to 45, wherein the pharmaceutical composition further comprises a pharmaceutically acceptable carrier.
47. The use of claim 46, wherein the pharmaceutically acceptable carrier is selected from the group consisting of poly(ethylene-co-vinyl acetate), PVA, partially hydrolyzed poly(ethylene-co-vinyl acetate), poly(ethylene-co-vinyl acetate-co-vinyl alcohol), a cross-linked poly(ethylene-co-vinyl acetate), a cross-linked partially hydrolyzed poly(ethylene-co-vinyl acetate), a cross-linked poly(ethylene-co-vinyl acetate-co-vinyl alcohol), poly-D,L-lactic acid, poly-L-lactic acid, polyglycolic acid, PGA, copolymers of lactic acid and glycolic acid, polycaprolactone, polyvalerolactone, poly (anhydrides),

copolymers of polycaprolactone with polyethylene glycol, copolymers of polylactic acid with polyethylene glycol, polyethylene glycol; and combinations and blends thereof.

48. The use of claim 46, wherein the pharmaceutically acceptable carrier comprises an aqueous gelatin, an aqueous protein, a polymeric carrier, a cross-linking agent, and a combination thereof.
49. The use of claim 46, wherein the pharmaceutically acceptable carrier comprises a matrix.
50. The use of claim 46, wherein the pharmaceutically acceptable carrier comprises at least one carrier selected from the group consisting of water, a pharmaceutically acceptable buffer salt, a pharmaceutically acceptable buffer solution, a pharmaceutically acceptable antioxidant, ascorbic acid, a low molecular weight pharmaceutically acceptable polypeptide, a peptide comprising about 2 to about 10 amino acid residues, a pharmaceutically acceptable protein, a pharmaceutically acceptable amino acid, an essential-to-human amino acid, a pharmaceutically acceptable carbohydrate, a pharmaceutically acceptable carbohydrate-derived material, a non-reducing sugar, glucose, sucrose, sorbitol, trehalose, mannitol, maltodextrin, dextrans, cyclodextrin, a pharmaceutically acceptable chelating agent, EDTA, DTPA, a chelating agent for a divalent metal ion, a chelating agent for a trivalent metal ion, glutathione, and pharmaceutically acceptable nonspecific serum albumin.
51. The use of any one of claims 30 to 50, wherein the pharmaceutical composition is sterile.
52. The use of any one of claims 30 to 50, wherein the pharmaceutical composition is sterilizable.
53. The use of any one of claims 30 to 50, wherein the pharmaceutical composition is sterilized.
54. The use of any one of claims 30 to 53, wherein the pharmaceutical

composition is in a vial in a unit dosage amount or in an integral multiple of a unit dosage amount.

55. The use of any one of claims 30 to 54, wherein the pharmaceutical composition is dried.
56. The use of any one of claims 30 to 54, wherein the pharmaceutical composition comprises a dehydrated matrix.
57. The use of any one of claims 30 to 54, wherein the pharmaceutical composition comprises a fusion protein in a lyophilized matrix.
58. Use of a pharmaceutical composition comprising a cell-permeable fusion protein conjugate comprising a polypeptidic cell-membrane transport moiety and a Clostridium botulinum C3 exotransferase unit, or a functional analog thereof, for the manufacture of a medicament for preventing or inhibiting uncontrolled proliferation and spreading or migration of a metastatic neoplastic cell of a cancer in a mammal.
59. Use of a pharmaceutical composition comprising a cell-permeable fusion protein conjugate comprising a polypeptidic cell-membrane transport moiety and a Clostridium botulinum C3 exotransferase unit, or a functional analog thereof, for the manufacture of a medicament for preventing or inhibiting uncontrolled proliferation and spreading or migration, within a resection margin of a host tissue proximal to the site of excision of a tumor of a cancer in a mammal, of a metastatic neoplastic cell residing in the resection margin.
60. Use of a pharmaceutical composition comprising a cell-permeable fusion protein conjugate comprising a polypeptidic cell-membrane transport moiety and a Clostridium botulinum C3 exotransferase unit, or a functional analog thereof, for the manufacture of a medicament for preventing growth of a tumor from a malignant cell in a host tissue in a mammal, wherein the fusion protein simultaneously prevents or inhibits at least two of malignant cell migration, malignant cell proliferation, angiogenesis or tubular structure formation or capillary network growth proximal to the malignant cell, and secretion of an

active metalloproteinase from the malignant cell.

61. Use of a pharmaceutical composition comprising a cell-permeable fusion protein conjugate comprising a polypeptidic cell-membrane transport moiety and a *Clostridium botulinum* C3 exotransferase unit, or a functional analog thereof, for the manufacture of a medicament for preventing growth within a resection margin of a host tissue proximal to a site of excision or removal of a first tumor of a cancer in a mammal, of a second tumor comprising a residual tumor cell of the cancer, wherein the fusion protein simultaneously prevents or inhibits at least two of residual tumor cell migration, residual tumor cell proliferation, angiogenesis or tubular structure formation or capillary network growth proximal to the residual tumor cell, and secretion of an active metalloproteinase from the residual tumor cell.
62. The use of any one of claims 58 to 61, wherein the fusion protein conjugate is BA-05.
63. The use of claim 58, 59 or 61, wherein the cancer is selected from the group consisting of breast, brain, colon, skin, kidney, and hepatic cancer.
64. The use of claim 63, wherein the cancer is a brain tumor selected from the group consisting of glial tumors, neuron tumors, pineal gland tumors, menigeal tumors, tumors of nerve sheath, lymphomas, malformative tumors, and metastatic tumors located in the brain derived from tumors of the lung, breast, melanoma, kidney, and gastrointestinal tract.
65. The use of claim 63, wherein the cancer is a brain tumor selected from the group consisting of anaplastic astrocytoma, glioblastoma multiform, pilocytic astrocytoma, oligodendroglioma, ependymoma, myxopapillary ependymoma, subependymoma, choroid plexus papilloma, neuroblastoma, ganglioneuroblastoma, ganglioneuroma, and medulloblastoma, pineoblastoma and pineocytoma, meningioma, meningeal hemangiopericytoma, meningeal sarcoma, Schwannoma (neurolemmoma) and neurofibroma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, primary and secondary subtypes of

Hodgkin's lymphoma, primary and secondary subtypes of non-Hodgkin's lymphoma, craniopharyngioma, epidermoid cysts, dermoid cysts and colloid cysts.

66. The use of any one of claims 58 to 65, wherein the pharmaceutical composition is formulated for a dosage form of about 0.001 micrograms per cc to about 50 micrograms per cc of tissue.

67. The use of any one of claims 58 to 65, wherein the pharmaceutical composition is formulated for a dosage form of about 0.0001 micrograms of fusion protein per cubic centimeter (cc) of tissue to about 100 micrograms per cubic centimeter of tissue.

68. The use of any one of claims 58 to 65, wherein the pharmaceutical composition is formulated for a dosage form of about 1 micrograms per milliliter to about 10 micrograms per milliliter to about 50 micrograms per milliliter.

69. The use of any one of claims 58 to 68, wherein the pharmaceutical composition is formulated for injection, topical application, or implantation.

70. The use of claim 1, any one of claims 58 to 68, wherein the pharmaceutical composition is formulated for an administration mode selected from the group consisting of intrarticular, intraocular, intranasal, intraneural, intradermal, intraosteal, sublingual, oral, topical, intravesical, intrathecal, intravenous, intraperitoneal, intracranial, intramuscular, subcutaneous, inhalation, atomization and inhalation, application directly into a tumor, application directly into a disease site, application directly on or into the margins remaining after resection of a tumor, enteral, enteral together with a gastroscopic procedure, and ECRP.

71. The use of any one of claims 58 to 70, wherein the polypeptidic cell-membrane transport moiety comprises a peptide containing from about 5 to about 50 amino acids.

72. The use of any one of claims 58 to 71, wherein the *Clostridium botulinum* C3 exotransferase unit comprises the amino acid sequence designated by the sequence of fusion protein BA-05.
73. The use of any one of claims 58 to 72, wherein the functional analog comprises a protein exhibiting activity in the range of 50% to 500% of that of wild type *Clostridium botulinum* C3 exotransferase.
74. The use of any one of claims 58 to 73, wherein the pharmaceutical composition further comprises a pharmaceutically acceptable carrier.
75. The use of claim 74, wherein the pharmaceutically acceptable carrier is selected from the group consisting of poly(ethylene-co-vinyl acetate), PVA, partially hydrolyzed poly(ethylene-co-vinyl acetate), poly(ethylene-co-vinyl acetate-co-vinyl alcohol), a cross-linked poly(ethylene-co-vinyl acetate), a cross-linked partially hydrolyzed poly(ethylene-co-vinyl acetate), a cross-linked poly(ethylene-co-vinyl acetate-co-vinyl alcohol), poly-D,L-lactic acid, poly-L-lactic acid, polyglycolic acid, PGA, copolymers of lactic acid and glycolic acid, polycaprolactone, polyvalerolactone, poly (anhydrides), copolymers of polycaprolactone with polyethylene glycol, copolymers of polylactic acid with polyethylene glycol, polyethylene glycol; and combinations and blends thereof.
76. The use of claim 74, wherein the pharmaceutically acceptable carrier comprises an aqueous gelatin, an aqueous protein, a polymeric carrier, a cross-linking agent, and a combination thereof.
77. The use of claim 74, wherein the pharmaceutically acceptable carrier comprises a matrix.
78. The use of claim 74, wherein the pharmaceutically acceptable carrier comprises at least one carrier selected from the group consisting of water, a pharmaceutically acceptable buffer salt, a pharmaceutically acceptable buffer solution, a pharmaceutically acceptable antioxidant, ascorbic acid, a low molecular weight pharmaceutically acceptable polypeptide, a peptide

comprising about 2 to about 10 amino acid residues, a pharmaceutically acceptable protein, a pharmaceutically acceptable amino acid, an essential-to-human amino acid, a pharmaceutically acceptable carbohydrate, a pharmaceutically acceptable carbohydrate-derived material, a non-reducing sugar, glucose, sucrose, sorbitol, trehalose, mannitol, maltodextrin, dextrans, cyclodextrin, a pharmaceutically acceptable chelating agent, EDTA, DTPA, a chelating agent for a divalent metal ion, a chelating agent for a trivalent metal ion, glutathione, and pharmaceutically acceptable nonspecific serum albumin.

79. The use of any one of claims 58 to 78, wherein the pharmaceutical composition is sterile.
80. The use of any one of claims 58 to 78, wherein the pharmaceutical composition is sterilizable.
81. The use of any one of claims 58 to 78, wherein the pharmaceutical composition is sterilized.
82. The use of any one of claims 58 to 81, wherein the pharmaceutical composition is in a vial in a unit dosage amount or in an integral multiple of a unit dosage amount.
83. The use of any one of claims 58 to 82, wherein the pharmaceutical composition is dried.
84. The use of any one of claims 58 to 82, wherein the pharmaceutical composition comprises a dehydrated matrix.
85. The use of any one of claims 58 to 82, wherein the pharmaceutical composition comprises a fusion protein in a lyophilized matrix.